



REVIEW

Patterns of Reactions to Red Pigment Tattoo and Treatment Methods

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ABSTRACT

Tattoos are common and used extensively as either body art or cosmetic make-up; more rarely, they can be traumatic in nature. We have systemically analysed the literature for the patterns of red pigment tattoo reactions and their treatment options. Our search identified 18 articles; there was 1 non-randomised controlled trial, and the rest were small case studies. In total 139 patients were included within the studies. This review systematically analyses the different subsets of red tattoo reactions including lichenoid, dermatitis, granulomatous, pseudolymphomatous and miscellaneous reactions. The current evidence for the treatment for the above is presented. Dermatitis and lichenoid reactions appear to be

the most common subtype of red pigment reactions with various treatment methods applied showing laser intervention to have some degree of success.

Keywords: Dermatitis; Granulomatous; Lichenoid; Pseudolymphomatous; Tattoos

INTRODUCTION

Tattoos are very popular in society today with their prevalence varying depending on the age group, ethnicity and location demographics, with the range thought to be between 5% to 40% in adults [1]. Tattoos can be classified as traumatic, cosmetic or decorative and their placement can be professional or amateur [2].

Complications of tattoos can be divided into cutaneous or systemic and can have an impact on the quality of life [3]. Cutaneous complications can occur either immediately or be delayed. Although there is no universally accepted classification, the complications are often classified according to the clinical and histological features with some overlap [4]. Examples of delayed reactions include allergic

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contact dermatitis, granulomatous dermatitis, lichenoid dermatitis and pseudolymphomatous reactions [4, 5].

In this article we discuss the different types of reactions to red tattoo pigment with a review of the literature with regards to the treatment for each pattern.

METHODS

A literature search was performed in November 2015 to review the current literature on red tattoo reactions in terms of classification and their treatments. A PubMed and Google scholar search was carried out with the search criteria “red tattoo”, “reaction”, “allergic” and “treatment”. Articles were selected depending on their relevance involving red tattoo reactions only. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

TYPES OF RED TATTOO PIGMENT (ORGANIC VERSUS INORGANIC)

Red tattoo pigment can be either organic or inorganic. Inorganic red pigment includes mercury, cadmium selenide and sienna (ferric hydrate) [6]. Organic red pigment includes sandalwood and brazilwood (or *Caesalpinia echinata*), both organic vegetable dyes [7, 8].

The red pigment can also be made with cinnabar (a mercury derivative) and it is this that is thought to cause the cell-mediated delayed hypersensitivity reaction [9]. Mercury in red tattoos has also been reported to cause lichenoid reactions [10] and rarely massive pseudoepitheliomatous hyperplasia [11].

Red tattoo pigments are thought to contain toxic metals, which predispose the skin to a

higher incidence of adverse reactions, particularly lichenoid and allergic contact dermatitis [8, 12, 13]. Swoden et al. studied the chemical composition of red pigment tattoos in 18 patients who developed cutaneous reactions and found aluminium, iron, calcium, titanium, silicon, mercury and cadmium within the pigment, all of which could trigger cutaneous inflammation [8].

One study tattooed pig and human skin with the pigment red 22 (commonly used and thought to be hazardous). The authors then extracted the pigment to assess the concentration in the skin and found high concentrations of the pigment (mean 2.53 mg/cm [3]), supporting the frequent incidence of complications from modern tattoos, particularly those involving red pigment [14].

Another study reviewed the histological pattern of skin biopsies from 19 patients who had red tattoo reactions. The majority (78%) of samples demonstrated dermatitis with evidence of T-lymphocytes and Langerhans cells, which further supports the presence of an allergic phenomenon [15].

PATTERNS OF RED TATTOO PIGMENT REACTIONS

Dermatitis

Eczematous reactions to red tattoos—alongside lichenoid—are the most common type of reaction observed, being either allergic contact dermatitis or photo-allergic dermatitis [16]. Photo-allergic reactions most commonly occur secondary to the cadmium subset of red pigment [17] and skin protection from ultraviolet light has been shown to exert protective effects [18].

One study in Denmark found that approximately half of sunbathers with red or black tattoos in particular suffered from photo-allergic reactions. They hypothesised that reactive oxygen species may play a role in triggering a dermatitis-type reaction in such individuals [19].

One interesting study carried out patch testing in 90 patients with tattoo reactions over a 4-year period. They found that red tattoo reactions did not predispose patients to have a positive patch test result with the common tested allergens. They hypothesised that the allergic result is due to haptens, possibly due to 'photochemical cleavage of red azo pigment' [20]. To strengthen the argument that patch testing does not correlate with red tattoo reactions, Anthony and Harland also found patch testing carried out prior to laser removal was negative to mercury at 48 and 96 h [21].

The exact understanding of the mechanisms behind the eczematous reactions observed in red tattoos is still lacking with type I–III hypersensitivity reactions playing a role [9]; however there is no conclusive evidence to date.

Lichenoid

In 1978 it was first hypothesised that tattoos may imitate a localised antigenic challenge, which in turn can cause a lichenoid pattern of reaction [22]. Lichenoid reactions in red organic tattoos have been shown to elicit a cytotoxic inflammatory response of the tissue [12] with lichenoid basal damage [23] thought to be produced by a delayed cellular hypersensitivity to metal particles [24].

The current consensus for the most common tattoo reaction is conflicting, with some papers stating dermatitis is the most common type, and others lichenoid [25]. Tattoo lichenoid

reactions are most commonly associated with red pigment, particularly because of mercury [26].

Pseudolymphomatous

Pseudolymphoma is a term given to a histological entity and has been reported to occur as a complication of tattoos that is histologically indistinct from malignant T- or B-cell lymphoma [4]; however the lymphoproliferative process is benign [27]. The clinical presentation is a pruritic plaque within the tattoo, often initially mistaken for lymphoma. The distinguishing factor between pseudolymphoma and lymphoma is the polyclonal nature of the lymphocytes [4]. Amann et al. propose it can only be distinguished from lymphoma with the aid of electron microscopy, immunohistochemistry and molecular biology [28].

In one reported case a 35-year-old male reacted with infiltrated nodules within the red areas of his tattoo 2 months post tattooing [29], whilst another paper reported a pseudolymphomatous allergic immune reaction 6 months post initial tattooing [30].

Granulomatous

Similar to lichenoid reactions, granulomatous reactions are thought to occur as a result of delayed hypersensitivity reactions to the presence of the red pigment [31].

One case study found a granulomatous reaction in the red pigment of four multi-coloured tattoos; interestingly only one of these lesions contained the metal mercury—which is thought to commonly cause these reactions in red tattoos [7].

Allopurinol has proved to be useful in the treatment of red tattoo granulomas, with

improvement of symptoms during a 6-month course and regression of results upon cessation of treatment [32].

Miscellaneous Reaction Patterns

Although dermatitis and lichenoid reactions are by far the most common, there have been reports of some rarer forms of reactions to red tattoo pigment. Litvinov and Sasseville reported a case of pyoderma gangrenosum [33] in a red tattoo consistent with the Koebner phenomenon. One group reported a red tattoo granulomatous dermatitis that was histologically similar to granuloma annulare presented post acquisition of a red pigment tattoo [31].

A 2003 paper found that the azo pigments and quinacridones found in red tattoo pigment led to skin reactions with differing histology found on biopsy: some lichenoid, some eczematous and others pseudolymphomatous [34] (Table 1).

There have also been several cases of systemic sarcoidosis presenting initially as a granulomatous tattoo reaction [35–38]. One study looked at sarcoid development within cosmetic tattooing of the eyebrows and lips and

observed that a granulomatous reaction containing a foreign body should not anticipate an exclusion of systemic sarcoidosis. A sarcoid within a tattoo is an example of the Koebner phenomenon [39]. Whether a sarcoid is a reaction to the tattoo itself or coincidental with a systemic disease remains a conundrum. It is suggested that in case of a tattoo sarcoid a search for systemic sarcoidosis is warranted [35].

Finally there are reports of deep-seated infections manifesting within tattoos, such as leprosy, syphilis, tuberculosis and *Mycobacterium chelonae* [40, 41].

TREATMENT OF RED PIGMENT REACTIONS

Multiple treatment options for red tattoo pigment reactions have been employed with little background evidence for their use. Medical treatment options have included allopurinol use as well as topical and intralesional corticosteroids [21] and secondary measures such as sun protection and antibiotics [18, 32, 42, 43]. Effective laser treatment has been demonstrated with both Q-switched Nd:YAG and erbium:YAG lasers [21, 44]. Anthony and Harland demonstrated successful laser

Table 1 Clinico-pathological patterns of red tattoo reactions

Skin reaction	Histology
Allergic contact dermatitis	Acanthosis, spongiosis, perivascular lymphocytic inflammatory infiltrate
Lichenoid dermatoses	Acanthosis and thickening of the stratum corneum
Granulomatous	Giant cell positive or negative
Pseudolymphomatous	T- or B-cell lymphoma equivalent
Pseudoepitheliomatous hyperplasia	Reactive changes: similar to SCC and keratoacanthoma
	Irregular acanthosis
	Low mitotic activity

treatment in seven patients within an open non-randomised clinical trial [21] and De Argila presented a successful outcome of one case of a lichenoid tattoo reaction treated with five treatment sessions of erbium:YAG [44].

A carbon dioxide (CO₂) laser has also been used. Kyanko et al. treated two cases of red tattoo dermatitis with a CO₂ laser in cases previously resistant to topical and intralesional corticosteroids [45]. Madan found that the CO₂ laser was particularly useful for red ink tattoo granulomas that were recalcitrant to conventional steroid treatment [46]. Of note, the CO₂ laser has also been reported to trigger the generalisation of localised tattoo dermatitis [47].

Finally, there is the option of surgical excision. The appropriateness of this will of course depend on the extent of the reaction and the size of the tattoo. Eczematous reactions have been successfully treated with excision and concomitant low-dose intralesional corticosteroids [43].

CONVENTIONAL METHODS OF TATTOO REMOVAL

Tattoo removal dates back to the Roman era when dried Spanish flies were used—the cantharides induced skin irritation and blistering [48]. Today nano- and picosecond lasers are the gold standard for removing tattoos of all types: professional, cosmetic or even traumatic [49]. Targeted photothermolysis is believed to create acoustic pressure leading to pigment fragmentation into the surrounding tissues and to enable it to be engulfed by macrophages leading to the subsequent removal of the pigment from the tattoo [22]. Although the treatment is largely safe,

depigmentation and occasionally scarring are potential long-term complications [50].

There have been reports of Q-switched lasers (nano-second) causing allergic reactions following their use in tattoo removal. This is thought to be due to the dispersion of the pigment triggering an immune response [9, 16]. Paradoxically, it is the Q-switched double-frequency Nd:YAG laser that is most beneficial for removing red pigment within tattoos. The current thinking of Q-switched laser treatment triggering an anaphylactic reaction has been challenged and dismissed by some [21].

RESULTS OF THE LITERATURE SEARCH

Our search identified 18 articles, with the majority being case studies. There was one open non-randomised controlled trial on lichenoid tattoo reactions, and the remainder were all case studies (Table 2). In total 139 patients were included within the studies. The red tattoo reactions described and treated included dermatitis (four case studies, overall $n = 23$), lichenoid (four case studies, one open non-randomised control trial, overall $n = 11$), granulomatous (three case studies, overall $n = 6$) and pseudolymphomas (two case studies, overall $n = 2$). Miscellaneous studies included a single case of pyoderma gangrenosum ($n = 1$), a case study on pigment darkening post Q-switched and pulsed laser treatment [including Q-switched Ruby, Q switched Nd:YAG and pulsed green dye (510 nm lasers) ($n = 5$)], a case of successful CO₂ laser removal of a facial red tattoo ($n = 1$) and a large study ($n = 90$) reviewing patch testing outcomes in patients with red tattoo reactions.

Table 2 Reported studies on red tattoo reactions

Study	Red tattoo reaction	Aim	No. of patients, <i>N</i>	Findings
Kyanko et al. [45]	Dermatitis	Case study	2	CO ₂ laser successfully treated erythema and pruritus in red tattoo dermatitis
England et al. [54]	Dermatitis	Case study	1	Nd:YAG laser-induced allergic reaction in tattoo removal
Jager and Jappe [55]	Dermatitis	Case study on nickel allergy	1	Red tattoo dermatitis responds to topical steroids
Hogsberg et al. [15]	Dermatitis	Review of histological pattern of skin biopsies in red tattoo reactions	19	78% of biopsies demonstrated dermatitis with T lymphocytes and Langerhans cell infiltration
Cruz et al. [7]	Granulomatous	Case study	4	Only 1 in 4 of red pigment granulomatous lesions contained mercury
Sweeney et al. [31]	Granulomatous	Case study	1	Granuloma annulare post red tattoo
Godinho et al. [32]	Granulomatous	Case study	1	Successful treatment with 6-month course of allopurinol
Bouchy et al. [29]	Pseudolymphoma	Case study showing 2-month delayed reaction	1	35-year-old male developed a 2-month delayed pseudolymphoma in red areas of tattoo
Jaehn et al. [30]	Pseudolymphoma	Case study	1	6-month delayed pseudolymphoma in tattoo, successfully treated with split thickness skin graft
Litvinov and Sasseville [33]	Pyoderma gangrenosum	Case study	1	Triggered by red tattoo dye
Taaffe et al. [22]	Lichenoid	Case study of laser treatment	1	Successful treatment with 8 sessions of Q-switched ND:YAG laser
Biro and Klein [43]	Lichenoid	Case study of steroid treatment	1	Cinnabar tattoo developed eczematous reaction 9 years post tattoo. Treated successfully with excision and 3-month low-dose topical steroids

Table 2 continued

Study	Red tattoo reaction	Aim	No. of patients, <i>N</i>	Findings
Dang et al. [42]	Lichenoid	Case study of steroid treatment	1	Successful halobetasol ointment treatment for lichenoid in red pigment areas of tattoo
Antony and Harland [21]	Lichenoid	Open non-randomised clinical trial of laser treatment	7	Lichenoid red tattoo responds to Q-switched 532 nm Nd:YAG laser after 6 sessions
De Argila et al. [44]	Lichenoid	Case study of laser treatment	1	Successful treatment of lichenoid red tattoo with 5 sessions of Er:YAG laser
Anderson et al. [55]	Pigment darkening	Case study	5	5 cases of irreversible ink darkening with Q-switched and pulsed laser treatment
Herbich [56]	Red tattoo	Case study	1	Successful removal of facial iron oxide tattoo with CO ₂ laser
Serup and Hutton Carlsen [20]	Red tattoo reactions in general	Report of results of patch testing in red tattoo reactions	90	Red tattoo reactions do not predispose patients to have a positive patch test with common allergens

Of the studies that reviewed treatment outcomes in red tattoo reactions, two were treated with topical steroids, two with CO₂ lasers, four with Q-switched Nd:YAG, one with Er:YAG, one with allopurinol, one with a split-thickness skin graft and one with surgical excision (Table 2).

DISCUSSION

Tattoos are popular and it is likely that reactions to tattoo pigment will continue to develop in various forms. Red pigment is the most common cause of reactions in tattoos and this can present in various clinical and histological variants with dermatitis and lichenoid being the most common. The literature on tattoo reactions, their classifications and treatments is not exhaustive. The high incidence of reactions in red tattoos is attributed to the toxic metals often found within the pigment, which predispose the skin to a higher incidence of adverse reactions [8, 12, 13]. Furthermore, there is no quality control or legislation regarding the inks contained within red tattoos [51], especially inorganic cinnabar tattoos, highlighting that a safer outcome may be found with synthetic tattoos whereby the dye within them is [21]. It has been reported that some inks have been obtained from the clothing industry (red dyes for clothes) and that there may have been batches contaminated in some way. One study analysed the decomposition of tattoo pigments using liquid chromatography and mass spectrometry; they found lasers broke down the pigments to produce 2-methyl-5-nitroaniline, 2,5-dichloraniline and 4-nitro-toluene. These materials are not only toxic but postulated to

be carcinogenic [52, 53], which may contribute to the high incidence of red tattoo reactions.

Most interestingly, the hypothesis that laser treatment for tattoo reactions can lead to anaphylaxis [9] has been challenged with successful improvement of lichenoid tattoo reactions in seven patients within one case study [21]. There have been promising results with both Q-switched Nd:YAG lasers and erbium:YAG [21, 22, 44] as well as successful outcomes with CO₂ lasers [45]. One could speculate that a type-1 anaphylactic reaction is unlikely to occur with the type 3 and 4 reactions demonstrated with red tattoo pigments. Another important point for clinicians to recognise is that patch testing does not correspond to the tattoo reaction outcome. All of the patch testing carried out by Anthony and Harland was negative, yet the patients had red tattoo reactions [21], suggesting that this step can be omitted with regards to clinical work-up. The evidence for this entire literature search, although enlightening, is based only on small case studies and therefore larger studies are required to cement these encouraging outcomes.

CONCLUSION

This review systematically analyses the different subsets of red tattoo reactions including lichenoid, dermatitis, granulomatous, pseudolymphomatous and miscellaneous reactions. Dermatitis and lichenoid reactions appear to be the most common subtype of red pigment reactions, with the various treatment methods applied showing laser intervention in fact to have positive outcomes, contrary to the hypothesis of anaphylaxis risk when it is used to treat red tattoo reactions.

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